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Introduction & aims: Oral azithromycin maintenance therapy is frequently prescribed in CF as it has been shown to improve long-term clinical outcome. However, systemic azithromycin use is associated with toxic effects. Entrapment of antimicrobial agents in liposomes has the potential to enable direct delivery to the site of infection in the lungs and to reduce toxic side-effects. Therefore, this study aimed to determine the antimicrobial activity of a novel liposomal azithromycin formulation against clinical respiratory isolates.

Methods: Antimicrobial activity of free azithromycin and azithromycin loaded liposomes against clinical *P. aeruginosa* and *S. aureus* isolates was determined using minimum inhibitory concentration (MIC)/ minimum bactericidal concentration (MBC), time-kill and biofilm assays. Liposomal uptake by isolates was determined using flow cytometry analysis.

Results: In general, there was no difference in MIC/MBC values for free and liposomal loaded azithromycin. The majority of *P. aeruginosa* and *S. aureus* isolates were resistant with MBCs ranging from 128 to >256 µg/ml and 8 to >256 µg/ml, respectively. However, liposomal azithromycin was significantly more potent than free azithromycin in both prevention of *P. aeruginosa* biofilm formation and eradication of *P. aeruginosa* biofilms. Liposomal uptake ranged from 57 to 96 % for *P. aeruginosa* and from 58 to 78% for *S. aureus*.

Conclusion: This novel liposomal azithromycin formulation could be potentially useful in the management of CF respiratory infection.

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